

REMARKS/ARGUMENTS

Upon entry of the present amendment, claims 20-35 will be pending in the application. Claims 1-19 have been canceled without prejudice. Claim 34 has been amended to properly letter sub-parts (a) through (e) consecutively. No new matter has been added by this amendment. Entry of the amendment is respectfully requested.

Each of the objections and rejections set forth in the Office Action mailed on October 3, 2003 is addressed individually below.

Restriction Requirement

The claims were subject to a two-way Restriction Requirement between Group I, system claims 1-19, and Group II, method claims 20-35. Applicants confirm the oral election of Group II, claims 20-35, without traverse, which was made in a telephone conversation between the undersigned and the Examiner on September 15, 2003. Non-elected claims 1-19 have been canceled without prejudice by the amendment submitted herewith.

Rejection of Claim 34 under 35 U.S.C. § 112, ¶ 2

Claim 34 was rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. The Office Action states that it is unclear how to interpret the phrase “the viability of an embryo” in claim 34, and asks what one of ordinary skill in the art would reasonably understand as being a viable embryo.

Applicants respectfully submit that the term “viability of an embryo” in claim 34 is clear in view of the description in Applicants’ specification and the ordinary meaning of the term “viable.” For example, the specification provides that “the invention can be used to assess the viability of an embryo by determining the flux of various analytes with respect to the embryo. ... With long-term embryo culture, the potential exists to profile biochemical parameters in each embryo in order to select for transfer only embryos of good development potential” (page 22, lines 8-14, emphasis added). The specification provides further that “the present invention ... allow[s] for the measurement of flux with respect to an embryo of various biologically significant molecules such as glucose. Since uptake of energy substrates is indicative of a healthy respiring embryo, these flux measurements allow for an assessment of the embryo’s viability” (page 22, lines 17-20, emphasis added). In addition, the results of experimental Example 5 in the specification are described as follows: “Current indicating glucose influx in

some mouse blastocysts is consistent with glucose metabolism by those cells. These results demonstrate the utility of self-referencing enzyme-based microsensors for assessing metabolism in single embryos in order to predict embryo viability” (page 31, lines 2-6, emphasis added).

The cited disclosure indicates that assessing the “viability of an embryo” means assessing the health or development potential of an embryo, as indicated by, *e.g.*, metabolism of glucose or other biologically significant molecules. This understanding of “viability of an embryo” is consistent with the plain meaning of the term “viable.” For example, Webster’s Third New International Dictionary, Merriam-Webster, Inc. (2002) defines “viable” as “capable of living” or “capable of growing or developing.” Thus, both Applicants’ specification and the ordinary meaning of the term “viable” make clear that “viability of an embryo” in claim 34 refers to the health or potential for growth or development of an embryo.

Therefore, Applicants respectfully submit that claim 34 is definite and, accordingly, request that the present rejection under 35 U.S.C. § 112, second paragraph, be reconsidered and withdrawn.

Rejection of Claims 20-21, 23-24, 27-33, and 35 under 35 U.S.C. § 102(a)

Claims 20-21, 23-24, 27-33, and 35 were rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Jung et al., Anal. Chem. 73:3759-3767 (2001) (“Jung”). The Office Action states that Jung was published on-line on June 30, 2001, and therefore qualifies as prior art under 35 U.S.C. § 102(a).

Applicants respectfully submit that Jung is not prior art with respect to the present application, because Jung was published less than one year prior to the application’s filing date, and the disclosure of Jung represents the inventive work of three of the co-inventors of the application. The authors of the Jung reference are Sung-Kwon Jung, James R. Trimarchi, Richard H. Sanger, and Peter J.S. Smith. The inventors of the present application are Sung-Kwon Jung, Richard H. Sanger, Peter J.S. Smith, and John R. Pepperell.

Submitted herewith is a Declaration of Peter J.S. Smith, Sung-Kwon Jung, Richard H. Sanger, and John R. Pepperell under 37 C.F.R. § 1.132, which states that the subject matter disclosed by the Jung reference represents the inventive work of Drs. Jung, Smith, and Sanger. As set forth in the Declaration, the fourth co-author of the Jung reference, Dr. Trimarchi, provided useful criticism during the progress of the published study, but did not make an

inventive contribution to the subject matter disclosed and claimed in the present application. In contrast, Dr. Pepperell, while not a co-author of the Jung reference, is a co-inventor of subject matter disclosed and claimed in the application. The inventors' Declaration setting forth these facts regarding authorship and inventorship establishes that Jung is not prior art to the present application under § 102(a).

Accordingly, because Jung is not prior art, claims 20-21, 23-24, 27-33, and 35 cannot be anticipated by Jung. Therefore, Applicants respectfully request that the present rejection under 35 U.S.C. § 102(a) be reconsidered and withdrawn.

Rejection of Claims 22 and 26 under 35 U.S.C. § 103(a)

Claims 22 and 26 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Jung in view of U.S. Patent No. 5,762,770 to Pritchard et al. ("Pritchard").

Applicants' claim 20 is directed to a method of determining a flux of an analyte using a self-referencing enzyme-based electrode. Claim 22 depends from claim 20, and specifies that the enzyme of the electrode is a dehydrogenase. Claim 23 depends from claim 20, and specifies that the enzyme is an oxidase. Claim 26 depends from claim 23, and provides that the enzyme is lactate oxidase and the analyte is lactate.

As described above, Applicants respectfully submit that Jung is not prior art, as established by the Declaration of the inventors submitted herewith.

Pritchard teaches an electrochemical biosensor test strip that may employ various enzymes to measure corresponding analytes (*e.g.*, glucose dehydrogenase to measure glucose, or lactate oxidase to measure lactate). (*See* Abstract; column 8, lines 55-57; Table 1). Pritchard does not teach or suggest a method of determining a flux of an analyte using a self-referencing enzyme-based electrode.

In the Office Action, it is argued that Jung teaches all of the limitations of claims 22 and 26, except the use of a dehydrogenase or lactate oxidase. The secondary reference, Pritchard, is asserted as teaching an alternate biosensor that employs glucose dehydrogenase to measure glucose, and can be modified to measure lactose using lactate oxidase. The Office Action asserts that it would have been obvious to use the teachings of Pritchard regarding dehydrogenase and lactose in the method of Jung.

To support a *prima facie* case of obviousness, the cited art must teach or suggest every element of the claimed invention. MPEP § 2142-2143.

Because the primary reference, Jung, is not prior art, Applicants respectfully submit that a *prima facie* case of obviousness cannot be established. The disclosure of Pritchard is directed to an electrochemical biosensor test strip, and does not teach or suggest a method of determining a flux of an analyte using a self-referencing enzyme-based electrode. Thus, Pritchard does not teach or suggest every limitation of claim 22 or 26.

Accordingly, because Jung is not prior art, and Pritchard does not teach or suggest every limitation of the claimed invention, *prima facie* obviousness has not been established. Therefore, claims 22 and 26 are not obvious over the cited art, and Applicants respectfully request that the present rejection under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

Rejection of Claim 25 under 35 U.S.C. § 103(a)

Claim 25 was rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Jung in view of U.S. Patent No. 5,643,721 to Spring et al. ("Spring").

As described above, Applicants' claim 20 is directed to a method of determining a flux of an analyte using a self-referencing enzyme-based electrode. Claim 23 depends from claim 20, and specifies that the enzyme of the electrode is an oxidase. Claim 25 depends from claim 23, and provides that the enzyme is glutamate oxidase and the analyte is glutamate.

Spring discloses an immobilization medium for immobilizing bioreagents to support materials. The immobilization medium can be used to produce an enzyme-based electrode (*e.g.*, a glucose oxidase electrode to measure glucose, or a glutamate oxidase electrode to measure glutamate). (*See* Abstract; column 6, lines 28-35; Examples 1 and 7). Spring does not teach or suggest a method of determining a flux of an analyte using a self-referencing enzyme-based electrode.

In the Office Action, it is argued that Jung teaches all of the limitations of claim 25 except the use of glutamate oxidase as the enzyme. The secondary reference, Spring, is asserted as teaching in an alternate biosensor that sensors for monitoring glucose can be modified to measure glutamate by using glutamate oxidase. The Office Action asserts that it would have been obvious to use the teachings of Spring regarding glutamate oxidase in the method of Jung.

Again, because the primary reference, Jung, is not prior art, Applicants respectfully submit that a *prima facie* case of obviousness cannot be established. The disclosure of Spring is focused on an immobilization medium, and does not teach or suggest a method of determining a flux of an analyte using a self-referencing enzyme-based electrode. Thus, Spring does not teach or suggest every limitation of claim 25.

Accordingly, because Jung is not prior art, and Spring does not teach or suggest every limitation of the claimed invention, *prima facie* obviousness has not been established. Therefore, claim 25 is not obvious over the cited references, and Applicants respectfully request that the present rejection under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

Rejection of Claim 34 under 35 U.S.C. § 103(a)

Claim 34 was rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Jung in view of U.S. Patent No. 6,062,225 to Keefe et al. ("Keefe").

Claim 34 is directed to a method of assessing the viability of an embryo by determining a flux of an analyte with respect to the embryo using a self-referencing enzyme-based electrode. The enzyme of the electrode contacts the analyte and generates a species detectable by the electrode.

Keefe discloses a method of determining the development potential of an embryo or oocyte by measuring the ion flux, preferably transmembrane steady-state calcium efflux, from the embryo or oocyte. The measurement is preferably made with a non-invasive ion-sensitive vibrating probe using a calcium ionophore. (*See* column 1, lines 26-32). Keefe does not teach or suggest determining the flux of an analyte using an enzyme-based electrode, whereby the enzyme of the electrode contacts the analyte and generates a species detectable by the electrode.

In the Office Action, it is argued that Jung teaches all of the limitations of claim 34 except the use of the sensor for determining embryo viability. It is asserted that Keefe discloses the use of analyte flux measurements to determine if embryos are morphologically capable of cleavage, and that it would have been obvious to use the teachings of Keefe with the method of Jung to assist in determining the relative health of a developing fetus.

Again, because the primary reference, Jung, is not prior art, Applicants respectfully submit that a *prima facie* case of obviousness cannot be established. The disclosure of Keefe is directed to determining ion flux, and does not teach or suggest the use of an electrode including

an enzyme, which contacts an analyte and generates a species detectable by the electrode. Thus, Keefe does not teach or suggest every limitation of claim 34.

Therefore, because Jung is not prior art, and Keefe does not teach or suggest every limitation of the claimed invention, *prima facie* obviousness has not been established. Accordingly, claim 34 is not obvious over the cited references, and Applicants respectfully request that the present rejection under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

Conclusion

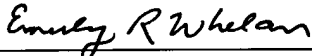
In view of the amendment and arguments presented above, and the attached declaration, Applicants respectfully submit that the rejections contained in the Office Action mailed on October 3, 2003 have been overcome, and that all of the pending claims are in condition for allowance.

This response is timely filed on January 5, 2004, as January 3, 2004 was a Saturday. No fees are believed to be due in connection with this correspondence. However, please charge any payments due or credit any overpayments to our Deposit Account No. 08-0219.

The Examiner is encouraged to telephone the undersigned at the number listed below in order to expedite the prosecution of this application.

Respectfully submitted,

Date: 1/5/04



Emily R. Whelan
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Boston, MA 02109
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Facsimile: (617) 526-5000



PATENTS

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appln. No. : 09/966,581 Confirmation No. 4006
Applicant : Jung et al.
Filed : September 28, 2001
TC/Art Unit : 1753
Examiner : K. Olsen
Docket No. : 58378.124
Title : Self-Referencing Enzyme-Based Microsensor and Method of Use
Customer No. : 23483

CERTIFICATION UNDER 37 C.F.R. § 1.8(a)

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below.

Jan. 05, 2004
Date of signature and
of mail deposit

Marghe Abbas for Maureen Di Vito
Maureen DiVito

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. § 1.132

Dear Sir:

We, Peter J.S. Smith, Sung-Kwon Jung, Richard H. Sanger, and John R. Pepperell
declare as follows:

1. We are the co-inventors of the above-referenced patent application ("the Application").
2. Sung-Kwon Jung, Peter J.S. Smith and Richard H. Sanger are also co-authors of a journal article entitled "Development and Application of a Self-Referencing Glucose

U.S.S.N. 09/966,581

PATENTS
Atty. Docket No. 58378.124

Microsensor for the Measurement of Glucose Consumption by Pancreatic β -Cells," Jung et al., Anal. Chem. 73:3759-3767 (2001) ("the Jung reference"), along with James R. Trimarchi. We are informed and believe that the Jung reference has been cited against the Application.

3. The subject matter disclosed in the Jung reference was invented by Peter J.S. Smith, Sung-Kwon Jung, and Richard H. Sanger.

4. James R. Trimarchi is named as a co-author of the Jung reference because he provided useful criticism during the progress of the study described therein. However, Dr. Trimarchi did not make an inventive contribution to the subject matter disclosed and claimed in the Application.

5. John R. Pepperell, while not a co-author of the Jung reference, is a co-inventor of subject matter disclosed and claimed in the Application.

We further declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Signed: _____
Peter J.S. Smith

Signed: _____
Richard H. Sanger

Dated: _____

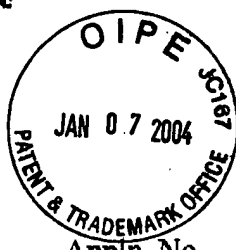
Dated: _____

Signed: 
Sung-Kwon Jung

Signed: _____
John R. Pepperell

Dated: Dec 19, 2003

Dated: _____



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5. John R. Pepperrell, while not a co-author of the Jung reference, is a co-inventor of subject matter disclosed and claimed in the Application.

We further declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Signed:


Peter J.S. Smith

Signed:


Richard H. Sanger

Dated:

22nd Dec. 2003

Dated:

Dec 23, 2003

Signed:

Sung-Kwon Jung

Signed:

John R. Pepperrell

Dated:

Dated:

John Pepperell, PhD - Boston_1798920_2.DOC

Page 1

PATENTS

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE



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Maureen DiVito for Maureen DiVito
Maureen DiVito

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John Pepperell, PhD - Boston_1798920_2.DOC

Page 2

U.S.S.N. 09/966,581

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Signed:

Richard H. Sanger

Dated:

Dated:

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Sung-Kwon Jung

Signed:

John R. Pepperell

Dated:

Dated:

12/29/03